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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/039,659	01/03/2002	Wei Wang	DX0589K1B	9741

7590 05/21/2003

DNAX Research, Inc.
901 California Avenue
Palo Alto, CA 94304-1104

EXAMINER
KEMMERER, ELIZABETH

ART UNIT	PAPER NUMBER
1646	7

DATE MAILED: 05/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

E.M.

Office Action Summary	Application No.	Applicant(s)	
	10/039,659	WANG ET AL.	
	Examiner	Art Unit	
	Elizabeth C. Kemmerer, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *43-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction

Applicant's election without traverse of Group VI (claims 33-38) in Paper No. 6 (10 April 2003) is acknowledged.

Status of Application, Amendments, And/Or Claims

The preliminary amendments filed 03 January 2003 (Paper No. 2) and 10 April 2003 (Paper No. 6) have been entered in full. Claims 1-42 are canceled. Claims 43-64 are directed to the elected invention and are under examination.

Sequence Rules

The instant application is not fully in compliance with the sequence rules, 37 CFR 1.821-1.825, because each disclosure of a sequence embraced by the definitions set forth in the rules is not accompanied by the required reference to the relevant sequence identifier (i.e., SEQ ID NO:). This happens at pp. 99-101, for example.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78).

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see pp. 99 and 100, for example). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The abstract of the disclosure is objected to because it consists of two paragraphs, and contains inappropriate information relating to the file history of the application. Correction is required. The second paragraph should be deleted. See MPEP § 608.01(b).

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following is suggested: "ANTIBODIES THAT BIND CHEMOKINE TECK".

35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 43-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear what is meant by the "mature" portion of the polypeptide. Neither the specification nor the art unambiguously define the term. Is the mature portion the polypeptide minus a leader sequence, or properly folded and active, or glycosylated?

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 58-61 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 58-61 recite Kd values of 100, 30, 10 and 3 **n**M, respectively. The specification as originally filed does not disclose these Kd values. At p. 34, lines 26-31, several Kd values are disclosed, but they are on the order of 100 to 3 μM. Applicant may wish to amend claims 58-61 to recite Kd values that appear at the specification at p. 34.

Claims 43-64 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the recited binding compositions and kits comprising same, wherein the binding compositions comprise **an antigen-binding site**

of an antibody that specifically binds **mammalian TECK protein**, does not reasonably provide enablement for the claimed inventions wherein the binding compositions are not related to antibodies, and wherein the TECK protein is defined as being 45% identical to the mature TECK protein shown in SEQ ID NO: 4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

There are two issues considered in this enablement rejection:

1) Scope of enablement of structures encompassed by the term "binding composition": The claims are directed to binding compositions and kits comprising same. The binding compositions are not defined structurally, and may be reasonably interpreted as encompassing receptors, organic compounds, etc. The specification only provides guidance regarding antibody-based binding compositions.

The instant fact pattern is similar to that in *In re Hyatt*, 708 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983), wherein a single means claim which covered every conceivable means for achieving the stated purpose was held nonenabling for the scope of the claim because the specification at most disclosed only those means known to the inventors. When claims depend on a recited property, a fact situation comparable to *Hyatt* is possible, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor. See also *Fiers v. Sugano*, 984 F.2d 164, 25 USPQ2d 1601 (Fed. Cir. 1993), and MPEP § 2164.08(a). The specification discloses sequences for mouse and human TECK proteins, and provides guidance regarding the generation of antibodies that specifically bind TECK proteins. However, no guidance is presented regarding other

types of binding compositions, such as receptors or organic molecules. Due to the lack of direction/guidance presented in the specification regarding binding compositions that are not based on antibodies, the absence of working examples directed to non-antibody based binding compositions, the complex nature of the invention, the unpredictability of what structures other than antibodies would specifically bind TECK, and the breadth of the claims which fail to recite structural limitations for the recited binding compositions, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

2) Scope of enablement of TECK proteins: The claims define the TECK protein structurally as a) the human TECK protein as defined by SEQ ID NO: 4, which is fully enabled; b) an antigenic fragment of human TECK protein of SEQ ID NO: 4, which is fully enabled; and c) a polypeptide that shares 45% sequence identity with human TECK protein of SEQ ID NO: 4. Part c) is what is deemed as only partially enabled. Part c) encompasses both naturally occurring TECK proteins, such as mouse and human TECK, but also numerous non-naturally occurring TECK protein variants, or muteins. The specification discloses mouse and human TECK proteins, which are chemokines. At p. 80 of the specification a working example is provided that demonstrates the chemotactic activity of TECK. While two mammalian TECK proteins are disclosed, no artificially generated TECK variants are disclosed. The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions

can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Bork, 2000, Genome Research 10:398-400; Skolnick et al., 2000, Trends in Biotech. 18(1):34-39, especially p. 36 at Box 2; Doerks et al., 1998, Trends in Genetics 14:248-

250; Smith et al., 1997, Nature Biotechnology 15:1222-1223; Brenner, 1999, Trends in Genetics 15:132-133; Bork et al., 1996, Trends in Genetics 12:425-427). Due to the large quantity of experimentation necessary to determine what structural features are requires for TECK activity, the lack of direction/guidance presented in the specification regarding muteins of mammalian TECK proteins, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite critical structural limitations or any functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 43-46, 49-51, 53-57 and 62-64 are rejected under 35 U.S.C. 102(e) as being anticipated by Wei et al. (US Patent 5,981,231).

Wei et al. disclose a binding composition (an antibody) that specifically binds a polypeptide having at least 45% identity to SEQ ID NO: 4 (chemokine β-15, Wei et al.'s SEQ ID NO: 2, which is 97.4% identical to the instantly recited SEQ ID NO: 2; col. 18, li. 9-19). Wei et al.'s chemokine β-15 has many long antigenic fragments in common with instantly claimed SEQ ID NO: 2. See alignment in Appendix A. Wei et al. teach the antibody as being conjugated to a chemical moiety (the chemiluminescent moiety disclosed at col. 26, li. 24-29); attached to a solid substrate (col. 23, li. 45-50, "immobilized antibody"); and detectably labeled (col. 25, last paragraph). Wei et al. disclose binding compositions which are polyclonal antibodies, monoclonal antibodies, Fab fragments and Fab2 fragments (col. 23, li. 9-13; col. 24, li. 38-42). Wei et al. teach the binding composition as an antibody that inhibits the protein's activity (col. 18, li. 9-14), which are suitable as pharmaceutical compositions which must be sterile (col. 30, li. 47-51). Wei et al. inherently teaches a kit comprising a container containing the binding composition when they disclose the ELISA assay, which is an antibody immobilized on a solid substrate, or container (col. 23, li. 29-44). Finally, Wei et al. teach a method of detecting a polypeptide in a sample comprising contacting a sample with the binding composition to allow a complex to form and detecting the complex (col. 23, li. 29-44).

35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject

matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 58-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wei et al. (U.S. Patent 5,981,231).

The disclosure of Wei et al. is summarized above.

Wei et al. do not specifically suggest Kd values for their binding compositions. However, such was a routine matter of screening and selecting, amounting to an optimization of parameters.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention as made to screen the antibodies disclosed by Wei et al. for specific Kd values with a reasonable expectation of success. The motivation would have been apparent to one of ordinary skill in the art, as routine in the process of selecting antibodies from a pool of newly generated antibodies for those with ordinary, desirable features.

The claimed invention as a whole was *prima facie* obvious over the prior art.

Claims 47, 48 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wei et al. (U.S. Patent 5,981,231) in view of Radka et al. (U.S. Patent 5,681,930).

The disclosure of Wei e al. is reviewed above.

Wei et al. do not teach binding compositions which specifically bind denatured protein, or which are Fv fragments.

However, such were routine in the art. For example, Radka et al. disclose antibodies that specifically bind the cytokine oncostatin which has been denatured by detergent (SDS; col. 13, li. 19-31). Radka et al. also disclose Fv forms of the antibody (col. 6, li. 45-49).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the antibodies disclosed by Wei et al. by obtaining antibodies that specifically bind denatured forms of the antigen protein or which re Fv forms as taught by Radka et al. with a reasonable expectation of success. The motivation to do so is given in Radka et al., who demonstrate the routine nature and desirability of having such forms of antibodies.

Thus, the claimed invention as a whole was *prima facie* obvious over the prior art.

Allowable Subject Matter

Claims limited to binding compositions comprise an antigen-binding site of an antibody that specifically binds the TECK protein of SEQ ID NO: 4 would be allowable.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D., whose telephone number is (703) 308-2673. The examiner can normally be reached on Mondays through Thursdays from 6:30 a.m. to 4:00 p.m. The examiner can also normally be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached on (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

ECK
May 19, 2003

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

Appendix A

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AAY41161
ID   AAY41161 standard; Protein; 149 AA.
XX
AC   AAY41161;
XX
DT   24-JAN-2000  (first entry)
XX
DE   Human chemokine beta-15 protein.
XX
KW   Chemokine beta-15 protein; CC chemokine protein; human.
XX
OS   Homo sapiens.
XX
PN   US5981231-A.
XX
PD   09-NOV-1999.
XX
PF   16-JUN-1997;   97US-0874460.
XX
PR   17-JUN-1996;   96US-0019837.
XX
PA   (HUMA-) HUMAN GENOME SCI INC.
XX
PI   Kreider BL,  Rosen CA,  Wei Y;
XX
DR   WPI; 1999-633320/54.
DR   N-PSDB; AAZ23250.
XX
PT   Nucleic acid encoding chemokine beta-15 -
XX
PS   Claim 1; Fig 1A-C; 30pp; English.
XX
CC   This represents a human chemokine beta-15 protein (a CC chemokine
CC   protein). The cDNA clone encoding the protein is contained in ATCC
CC   Deposit No. 97519. The protein can be expressed by standard recombinant
CC   methodology. Chemokine beta-15 can be used in the treatment of
CC   individuals in need of increased levels of chemokine beta-15 activity in
CC   the body, by administering a composition comprising the isolated
CC   chemokine beta-15 polypeptide.
XX
SQ   Sequence   149 AA;

  Query Match             97.4%;  Score 775.5;  DB 20;  Length 149;
  Best Local Similarity   98.7%;  Pred. No. 1.8e-85;
  Matches  148;  Conservative    0;  Mismatches    1;  Indels    1;  Gaps    1;

Qy       1 MNLWLLACLVAGFLGAWAPAVHTQGVFEDCCLAYHYPIGWAVLRRAWTYRIQEVSGSCNL 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 MNLWLLACLVAGFLGAWAPAVHTQGVFEDCCLAYHYPIGWAVLRRAWTYRIQEVSGSCNL 60

Qy      61 PAAIFYLPKRHRKVCGNPKSREVQRAMKLLDARNKVFAKLHHNMQTFQAGPHAVKKLSSG 120
           |||||||||||||||||||||||||||||||||||||||||| |||| ||||||||||
Db      61 PAAIFYLPKRHRKVCGNPKSREVQRAMKLLDARNKVFAKLHHNTQTFQ-GPHAVKKLSSG 119

Qy     121 NSKLSSSKFSNPISSSKRNVSLLISANSGL 150
           |||||||||||||||||||||||||||||||
Db     120 NSKLSSSKFSNPISSSKRNVSLLISANSGL 149
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